LEGAL ISSUES IN CLINICAL RESEARCH

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OBJECTIVES

1. Discuss the history and elements of informed consent for clinical and research care.

2. Summarize the evolution and types of advance directives and other surrogate-decision making requirements.

3. Comment on some legal issues surrounding the involvement of children in research.

4. Discuss issues related to medical records including documentation requirements and protection of confidentiality.

5. Discuss issues of legal liability and coverage for Federal employee and non-Federal clinical researchers.

6. Understand the rules and criteria in order to identify and resolve conflicts of interest.

7. Describe the policies and issues associated with authorship and rights in data.

CONTENT OUTLINE

I. Introduction

A topic such as legal issues in clinical research is expansive and cannot be fully explored in a few hours or even a few days. An attempt has been made to focus on issues commonly encountered by, or of concern to, investigators in the clinical research environment.

II. Informed Consent

A. Where did the idea come from that a patient has the right to reasonably informed participation in decisions involving his or her health care? Historically, informed consent grew from the common law tort of battery, i.e., an individual's right to be protected from nonconsensual touching.

B. Early cases looked only to the existence of a consent. Beginning in the 1950s, courts began to focus on the "quality" of the consent, i.e., finding no legally effective consent unless the patient understands the procedure or treatment to which he or she is consenting and the risks inherent therein.

C. Generally, the case law has developed so as to provide for disclosure of the following items, when applicable:

1. diagnosis (patient's condition or problem)
2. nature and purpose of the proposed treatment
3. risks and consequences of proposed treatment
4. probability of success
5. feasible alternatives
6. prognosis if the proposed treatment is not given

D. These general elements of clinical care or treatment consent are closely related to those elements necessary in a consent for participation in research as required by 45 CFR section 46.116, the human subject protection regulations.

E. A competent patient or the duly authorized legal representative signs a variety of consents, e.g., protocol consents, a general admission consent and consents for certain medical and surgical procedures. Such consents should incorporate the necessary, applicable elements of informed consent. There is an exception from the informed consent requirement for the provision of clinically accepted care in an emergency, unless the patient is competent and refusing.

III. Advance Directives/Substitute Consent

A. Today it seems implicit that if an individual has the right to consent to treatment that same individual has the right to refuse certain procedures or treatments. But what happens when the individual lacks the capacity to consent (or refuse)? Several questions arise, for example, who will make the decision and how can the individual's wishes be taken into account.

B. Since the Quinlan decision in 1976, a number of court cases have upheld the right of a competent patient to refuse treatment even if it is life-sustaining, and courts or state laws have authorized family members or other designated individuals to act as surrogate decision makers for incompetent patients. However, the U.S. Supreme Court in Cruzan upheld Missouri's requirement that clear and convincing evidence of a patient's wishes was necessary in order for a surrogate to forego or withdraw life-sustaining treatment in the case of a young woman in a persistent vegetative state, given the absence of a clear statement or appointment of a proxy by the patient. Because of the case law and related statutory developments, attention has been focused on the use of advance directives, documents either clearly reflecting the patient's wishes and/or designating a substitute decision maker.

C. There are two general types of legally recognized advance directives, the living will and the durable power of attorney for health care.

1. Living Will - a document that permits an individual to direct in writing that certain life-sustaining measures be withheld or withdrawn if he or she is in a "terminal condition" and doesn't have the capacity to make decisions.

2. Durable Power of Attorney for Health Care (a.k.a. DPA or "health care proxy") - a document in which an individual appoints a surrogate to make decisions in the event he or she becomes incapable. The DPA may or may not contain statements of the person's wishes to guide the surrogate.

D. The Clinical Center (CC) has its own DPA form which provides for the appointment of a surrogate who is authorized to provide informed consent for participation in research and routine medical care while the individual is at the CC. The CC recognizes other advance directives validly executed by the patient. Depending on the nature of the research or the process of the disease being studied, execution of a DPA may be required for participation.

E. What happens when a patient has not executed an advance directive and becomes mentally incapacitated? If the individual previously expressed wishes which are documented in the medical record, those wishes may be followed. Generally, in the absence of a DPA or judicially appointed guardian, certain individuals are authorized by State law to give "substituted consent" for the furnishing (as opposed to withdrawal) of medical or dental care.

IV. Children in Research

A. While children may be required to assent to their participation in research, they cannot provide legally valid consent. Except as provided in the human subject protection regulations, a child requires the permission of both parents or his or her legal guardian to participate in research. A child is defined as a person who has not attained the legal age for consent to research treatments or procedures, under the applicable law of the jurisdiction in which the research will be conducted. At the CC, anyone who is under age 18 cannot provide legally effective consent unless the individual is married or a parent.

B. Determining who has the legal authority to provide consent in the case of a child in foster care calls for careful investigation. States differ as to who may provide consent for a foster child to participate in research. Increasingly,

the State agency responsible for placement of the child or a judge will need to be involved in the research consent process.

C. By regulation, institutional review boards are required to ascertain that adequate provisions are made for soliciting the assent of children who are capable of providing assent or that assent is not required due to the limited capability of the children involved or the prospect of direct benefit from their participation in the research.

D. If parents refuse to consent to the child's participation in research, that decision would govern. However, if parents refuse the provision of ordinary medical care in which the benefits outweigh the risks, the State will ordinarily step in, e.g., in the case of a parent's refusal to permit a life-sustaining blood transfusion on religious grounds.

V. Medical/Research Records

A. Complete and accurate medical or research records are not only necessary to provide quality care to patients and insure scientific integrity and verification but also become the most essential evidence in the event of litigation, review, audit or other inquiry.

B. There are three basic rules:

1. Documentation should be complete.
2. Documentation should be accurate.
3. Entries should be timely.

C. How can the record be corrected? Entries should never be obliterated or removed. If correction is needed, a line should be drawn through the incorrect entry, the correct information entered, initialed and dated. If this is not possible, the incorrect entry should be lined out and an explanation of the change, should be written as close as possible to the original entry, signed and dated. Corrections should only be made by the original author; if not possible, correction to a medical record should be made by a Senior Medical Staff member.

D. Federal statutes, regulations and CC policy place clear responsibility on health care professionals to safeguard patient confidentiality and patient records. Under the Privacy Act, 5 USC §552a et seq., disclosure of any information from a patient's medical record, except to another NIH employee who has a need to know the information in order to perform his or her job, may not be made without the patient's consent, unless one of the exceptions to the Privacy Act applies.

E. The Privacy Act applies to all Government records, not just medical records, that contain information on individuals and are filed so that the records are retrieved by use of the person's name or some other personal identifier. The Privacy Act applies to personal information stored in computers as well as manual files. Violations of the Privacy Act, such as improper disclosures or maintenance of a system of records without proper notice, can carry both civil and criminal penalties. Individuals, who wish to establish a system of records, need to consult with their records management officer.

VI. Legal Liability/Malpractice Coverage

A. The Federal Tort Claims Act, 28 USC §2671 et seq., generally provides that the United States shall be liable for property injury or loss and personal injury or death caused by the negligence, wrongful act or omission of any employee of the Government while the employee is acting within the scope of his or her office or employment. Section 224 of the Public Health Service Act, 42 USC §233, generally provides that the Federal Tort Claims Act is the exclusive remedy available to an individual injured as the result of negligence of an officer or employee of the Public Health Service while providing health care within the scope of his or her employment. These provisions operate to limit the naming of individuals as defendants in civil lawsuits and require that the Government be substituted as a party.

B. The Federal Government self-insures. Professional liability insurance is, therefore, not maintained for Federal employees. Clinical researchers at the NIH are subject to actions for negligence or malpractice with less frequency than other health professionals not involved in research. The types of claims filed most commonly involve allegations of mistakes in treatment or diagnosis or defects in informed consent. Health professionals, who are not Federal employees and working at the CC, are required to be insured and to maintain professional liability insurance with designated coverage amounts similar to outside investigators.

C. Drug and technology development companies, and others, often ask investigators interested in receiving materials or doing collaborative studies with them to provide an assurance that the Government will indemnify them for any costs in the event something goes wrong. Absent express statutory authority, the Federal government may not enter into an agreement to indemnify where the amount of the Government's liability is indefinite, indeterminate or potentially unlimited. Extramural researchers may consider purchasing project casualty or liability insurance.

VII. Conflict of Interest

A. Pursuant to statute and implementing regulations, Federal employees are prohibited from participating in an official capacity in matters affecting their own financial interests or the financial interests of other specified persons or organizations. If the interest is disclosed and it is determined to be not so substantial as to be deemed likely to affect the integrity of the services provided by the employee, a waiver may be granted. If not, disqualification may be required.

1. Situations Involving Possible Conflicts of Interest

a. Employment Negotiations
b. Stock Holdings
c. Acquisition Situations
d. Outside Activities
e. Gifts

B. As described in 42 CFR Part 50, Subpart F, Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding Is Sought, NIH grantees are required to establish safeguards to prevent employees or consultants from using their positions for purposes that are, or give the appearance of being, motivated by a desire for private financial gain for themselves or others such as those with whom they have family, business or other ties. Institutions receiving financial support must have written policy guidelines on conflict of interest and its avoidance and provisions for dealing with conflicts of interest.

VIII. Authorship/Rights in Data

A. Authorship questions are ordinarily resolved by the research group, Laboratory or Branch, and the primary author. Although there are no legal requirements governing who may or may not claim authorship of a scientific article, professional standards and NIH policy require that the designation of authorship should be based on a significant contribution to the conceptualization, design, execution, and/or interpretation of the research study. Authors also must be willing to take responsibility for the study and to support the general conclusions of the study. Lesser contributions are often handled by acknowledgment.

B. Data management, including the decision to publish, is the responsibility of the principal investigator. Research data and supporting materials, such as unique reagents, of NIH investigator/employees belong to the NIH and should be maintained in the Laboratory in which they are developed. Ownership of data, in this case by NIH, generally carries with it the right to decide whether or not to disclose the data and to control its use. Departing investigators, with

approval, may take copies of notebooks or other materials for further work. Certain restrictions related to patient privacy, prepublication and intellectual property may obtain to the copying of clinical and other research data.

C. NIH investigators may receive requests for data or records from subjects, under the Freedom of Information Act, or pursuant to legal process such as subpoena or discovery request. If the information is contained in a Privacy Act system of records, i.e., retrieved by a personal identifier, the person whose file it is may authorize release of the information. Requests for data in NIH records under the Freedom of Information Act or pursuant to legal process are releasable subject to a number of exceptions. Prepublication data, nongovernmental trade secrets or proprietary information, and personal private information are ordinarily protected from public release.

D. If the NIH sponsors extramural research, who owns the data? Ownership of data depends on the funding mechanism and the terms of the award. Generally, for grants, the grantee owns the data in the absence of a specific grant condition to the contrary. In the case of contracts and cooperative agreements, ownership of data is dependent on the terms of the award. Ownership of the data does not operate to preclude access to the data by NIH.

RECOMMENDED READING:

NIH Durable Power of Attorney for Health Care Decision Making (1994)

State of Maryland Living Will and Advance Directive Forms

Levine, R. (1986). Ethics and Regulation of Clinical Research, 2nd ed. New Haven: Yale University Press, Chapters 5 and 10.

U.S. Dept. of Health and Human Services' Publication,"Privacy Act"

Section 45-17-10 of PHS General Administration Manual, Privacy Act "Relationship to the Freedom of Information Act"

"Guidelines for the Conduct of Research at the NIH"

Marcia Barinaga, Who Controls a Researcher's Files? Science, Vol. 256, 1620-21(June 19, 1992).

Publishing Sensitive Data: Who Calls the Shots? Science, Vol. 276, 523-26 (April 25, 1997) - articles by Wade Roush, Eliot Marshall and Gretchen Vogel